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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILSON, MICHAEL C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/797,371	KATZ ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2008*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-42,44,45,47,48,57,160-162 and 169-186* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-42, 44, 45, 47, 48, 57, 160-162 and 169-186* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-5-09&5-27-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner in this application has changed. Please send future correspondences to Examiner Michael C. Wilson, Art Unit 1632.

Applicant's arguments filed 9-23-08 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-38, 43, 46, 49-56, 58-159, 163-168 have been canceled. Claims 183-186 have been added. Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-186 are pending and under consideration.

This action is non-final in view of the new "new matter," indefiniteness and art rejections below.

Specification

The title of the application must be changed to indicate the claims are drawn to a method of differentiation.

Claim Rejections - 35 USC § 112

New Matter

Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-186 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

Differentiating the stem cells into "two or more" developmental phenotypes such as adipogenic, osteogenic, chondrogenic and myogenic has support on pg 3, lines 15-17, and on pg 18-19.

The concept of differentiating adipose stem cells into at least two cell types selected from the group consisting of "fat, bone, cartilage and muscle cells" using "adipogenic, osteogenic, chondrogenic or myogenic media" in claims 39 and 160 is new matter. The claims encompass differentiating stem cells obtained from adipose tissue into mature, fully differentiated fat, bone, cartilage or muscle cells as encompassed by the claims. However, the specification is limited to differentiating stem cells derived from adipose into cells having adipogenic, osteogenic, chondrogenic or myogenic potential; not fully differentiated cells as now claimed. Differentiating stem cells into cells having adipogenic, osteogenic, chondrogenic or myogenic potential as described on pg 18-20 has a different scope than differentiating stem cells into fat, bone, cartilage and muscle cells as claimed because cells having adipogenic, osteogenic, chondrogenic or myogenic potential have a different structure than mature, fully differentiated fat, bone, cartilage or muscle cells as encompassed by the claims. Pg 20, lines 12-18, teaches one clonal stem cell derived from adipose that differentiated into bone, fat, cartilage and muscle tissue and other clones that were able to differentiate into at least three types of tissue. It appears the cells on pg 20 have adipogenic, osteogenic, chondrogenic or myogenic potential because they are described as tissue

and not described as being fully differentiated, mature fat, bone, chondrocytes or muscle cells as claimed. It is not readily apparent that the cells on pg 20 are fat, bone, cartilage or muscle cells as claimed. Therefore, the specification does not support the concept of differentiating stem cells derived from adipose into "fat, bone, cartilage and muscle cells" as claimed.

The claims as written encompass differentiating at least two cell types from one type of media. However, the specification is limited to differentiating stem cells derived from adipocytes into cells having adipogenic potential using adipogenic media, into cells having osteogenic potential using osteogenic media, into cells having chondrogenic potential using chondrogenic media and into cells having myogenic potential using myogenic media. The specification does not support the concept of differentiating stem cells derived from adipocytes into at least two cell types selected from the group consisting of cells having adipogenic, osteogenic, chondrogenic or myogenic potential using adipogenic, osteogenic, chondrocytic or myogenic media as broadly claimed. The concept of differentiating two types of cells from adipogenic, osteogenic, chondrocytic or myogenic media is a broader concept than those originally described by applicants and is new matter.

The concept of differentiating clonally isolated stem cells obtained from adipose tissue on a lattice as in claims 174-178 is new matter. The specification contemplates putting cells of the invention onto a lattice for use in treatment (pg 12, last 3 lines), but the specification does not contemplate differentiating the cells on a lattice as claimed. Accordingly, the claims are new matter.

New claims 183-186 are new matter. Applicants state support is found in the claims and specification originally filed. The limitations in the claims cannot be found in the specification or claims originally filed.

Written Description

The rejection regarding written description for "stem cells… …obtained from adipose tissue" made on 5-5-06 and maintained in the office action sent 5-23-08 has been withdrawn because the specification taught how to isolate stem cells from adipose tissue such as lipoaspirate and that cells derived from the adipose tissue were pluripotent, i.e. stem cells.

Enablement

Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-186 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method of differentiating clonally isolated stem cells obtained from adipose tissue comprising: culturing clonally isolated stem cells obtained from adipose tissue under conditions sufficient for the stem cells to differentiate into cells having adipogenic, osteogenic, chondrogenic or myogenic potential, wherein the stem cells have telomeric activity, does not reasonably provide enablement for culturing clonally isolated stem cells obtained from adipose tissue under conditions sufficient for the stem cells to differentiate into at least two cell types selected from the group consisting of fat, bone, cartilage or muscle cells using adipogenic, osteogenic, chondrogenic or myogenic media as broadly claimed. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 39 and 160 are drawn to a method of differentiating clonally isolated cells having telomeric activity obtained from adipose tissue wherein the stem cells differentiate into cells of any two or more of a fat, bone, cartilage, or muscle cell comprising culturing the stem cell in adipogenic, osteogenic, chondrogenic, or myogenic morphogenic medium under conditions sufficient for the cell to differentiate.

The specification does not enable those of skill to determine the conditions required to differentiate a stem cell isolated from adipose tissue into any of two more cells selected from the group consisting of fat cell, bone cell, cartilage cell, and muscle cell using adipogenic, osteogenic, chondrogenic or myogenic media as broadly claimed.

Pg 18 teaches adipogenic, osteogenic, myogenic and chondrogenic media. Pg 18, line 26, teaches adipose derived stem cells in chondrogenic media have chondrogenic potential. The specification does not teach they become chondrocytes as claimed.

Pg 18, line 28, teaches adipose derived stem cells in adipogenic media have adipogenic potential (pg 19, line 4). The specification does not teach they become adipocytes as claimed.

Pg 19, line 6, teaches adipose derived stem cells in osteogenic media have osteogenic potential (line 11). The specification does not teach they become bone cells as claimed.

Pg 19, line 12, teaches adipose derived stem cells in myogenic media have myogenic potential (line 11). The specification does not teach they become muscle cells as claimed.

Pg 19, lines 25-30, teaches 5-azacytidine did not induce differentiation of the stem cells into cells with myogenic potential.

One clonal cell line was able to differentiate into bone, fat, cartilage and muscle when exposed to the respective media. A number of clones were able to differentiate into three types of tissue (pg 20, lines 13-16).

The stem cells that differentiate into cells having adipogenic, osteogenic, chondrogenic and myogenic potential as described on pg 18-19 are not fat cells, bone cells, chondrocytes or muscle cells as claimed. Cells with adipogenic, osteogenic, chondrogenic and myogenic potential as described on pg 18-19 have a different structure than mature, fully differentiated fat, bone, chondrocytes or muscle cells as claimed.

The clonal stem cells that differentiated into fat, bone, cartilage and muscle described on pg 20 are not fat, bone, cartilage and muscle cells as claimed because they merely have adipogenic, osteogenic, chondrogenic and myogenic potential as described on pg 18-19. It appears from pg 20, lines 12-18, the clonal stem cells were cultured in adipogenic, osteogenic, chondrogenic and myogenic morphogenic medium and were able to differentiate into cells having adipogenic, osteogenic, chondrogenic or myogenic potential as similarly described on pg 18-19. It is not readily apparent that the clonal stem cells on pg 20, lines 12-18, differentiated into fat, bone, cartilage and

muscle cells as claimed. If applicants actually did obtain fat, bone, chondrocyte and muscle cells from the clonal stem cells on pg 20, the specification fails to teach the parameters required to differentiate cells beyond those having adipogenic, osteogenic, chondrogenic and myogenic potential as described on pg 18-19 into fat, bone, chondrocytes and muscle cells.

The specification does not enable those of skill to differentiate stem cells into two types of cell using any adipogenic, osteogenic, chondrogenic or myogenic media as broadly claimed. The claims as written encompass differentiating the at least two cell types from one type of media. However, the specification is limited to differentiating stem cells derived from adipocytes into cells having adipogenic potential using adipogenic media, into cells having osteogenic potential using osteogenic media, into cells having chondrogenic potential using chondrogenic media and into cells having myogenic potential using myogenic media. The specification does not teach how to differentiate stem cells derived from adipocytes into at least two cell types selected from the group consisting of cells having adipogenic, osteogenic, chondrogenic or myogenic potential using adipogenic, osteogenic, chondrocytic or myogenic media as broadly claimed. It would have required those of skill undue experimentation to determine how to differentiate stem cells into at least two types of cell using one type of media as broadly claimed.

Claim 48 is not enabled because the specification fails to teach the conditions required to differentiate clonally isolated stem cells obtained from adipose tissue in vivo. Nowhere can such conditions be found in the specification or the art at the time of filing.

Accordingly, it would have required those of skill undue experimentation to determine the parameters required to target the stem cells in vivo such that differentiation into at least two cell types would occur.

Claims 174-178 are not enabled because the specification does not teach differentiating clonally isolated stem cells obtained from adipose tissue on a lattice. The specification contemplates putting cells of the invention onto a lattice for use in treatment (pg 12, last 3 lines), but the specification does not contemplate differentiating the cells on a lattice as claimed. It would have required those of ordinary skill undue experimentation to determine the parameters of how to differentiate the cells claimed when they were part of a lattice.

Indefiniteness

Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-182 remain and claims 183-186 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record as set forth in the office action mailed on May 5, 2006.

Claims 39 and 160 are indefinite because the steps and reagents of the method are not clearly set forth. It is unclear if the two or more cell types selected from the group consisting of fat cell, bone cell, cartilage cell, and muscle cell can result by culturing stem cells obtained one type “of adipogenic, osteogenic, chondrogenic and myogenic morphogenic medium.” It is unclear if the claim is intended to encompass

culturing the stem cell in one type of medium such that at least two types of cells are differentiated.

Claims 39 and 160 are indefinite because do not clearly set forth the steps of the method. Most of the preamble includes functional limitations that belong in the body of the claim; the body of the claim should clearly set forth the positive method steps required to perform the method. "A method of differentiating clonally isolated stem cells obtained from adipose tissue comprising culturing clonally isolated stem cells obtained from adipose tissue such that differentiation into… …occurs, wherein the clonally isolated stem cells have telomeric activity" would clearly set forth the method step required to perform the method.

Claims 39 and 160 are indefinite because the metes and bounds of "telomeric activity" are unclear. If applicants intend the phrase to mean the stem cells have telomerase activity, the claim should clearly state the stem cells express functional telomerase or have telomerase activity. However, it is unclear how the phrase further limits the stem cells because all adult cells express telomerase at low levels in a cycle-dependent manner.

Claim 40 is indefinite because it does not clearly further limit the medium. The phrase "wherein the medium is adipogenic, osteogenic, chondrogenic or myogenic" would be clear.

Claim 41 is indefinite because it does not clearly further limit the medium to adipogenic medium. The phrase "wherein the medium is adipogenic" would be clear. Claim 41 is indefinite because it is unclear how two types of cells can differentiate using

only adipogenic medium. Claim 41 is also indefinite because it does not clearly set forth the cell obtained is a fat cell. Clarification is required.

Claim 42 is indefinite because it does not clearly further limit the medium to chondrogenic medium. The phrase "wherein the medium is chondrogenic" would be clear. Claim 42 is indefinite because it is unclear how two types of cells can differentiate using only chondrogenic medium. Claim 42 is also indefinite because it does not clearly set forth the cell obtained is a cartilage cell. Clarification is required.

Claim 44 is indefinite because it does not clearly further limit the medium to myogenic medium. The phrase "wherein the medium is myogenic" would be clear. Claim 44 is indefinite because it is unclear how two types of cells can differentiate using only myogenic medium. Claim 44 is also indefinite because it does not clearly set forth the cell obtained is a muscle cell. Clarification is required.

Claim 45 is indefinite because it does not clearly further limit the medium to osteogenic medium. The phrase "wherein the medium is osteogenic" would be clear. Claim 45 is indefinite because it is unclear how two types of cells can differentiate using only osteogenic medium. Claim 45 is also indefinite because it does not clearly set forth the cell obtained is a bone cell. Clarification is required.

Claim 48 is indefinite because a clonally isolated stem cell cannot be differentiated in vivo. Clarification is required.

Claim 57 is indefinite because the metes and bounds of what applicants consider a defined cell population are wholly unclear. The specification does not define such a

population; therefore, those of skill would not know when a “defined” cell population had been obtained.

Claim 161 is indefinite because the metes and bounds of what applicants consider a "conditioned medium of a specific cell type" are unclear. It cannot be determined how the phrase further limits claim 160, what kinds of media are "specific" or when a media is no longer “specific.”

Claim 169 is indefinite because it further limits the “muscle cell” but only lists muscles. The phrase “wherein the muscle cell is a skeletal muscle cell, cardiac muscle cell, or a smooth muscle cell” would be clear.

Claim 170 is indefinite because the metes and bounds of proteins “specific” for muscle are unclear.

Claim 172 is indefinite because it is unclear if “the cell” refers to the stem cell, fat cell, muscle cell, etc. claim 172 is also indefinite because the cell cannot differentiate into a fat, bone, muscle, etc. cell as in claim 39 but only differentiate into a fat, bone or muscle precursor cell as in claim 172. Claim 39 requires the stem cell has already differentiated past the "precursor” stage. If applicants are attempting to further limit the fat cell, bone cell, etc., please clearly further limit the fat cell, bone cell, etc.

Claims 179-180 are indefinite because in is unclear whether “the cell” refers to the stem cell or the derived cell.

Claim 181 is indefinite because the step is not clearly set forth and because the limitation does not further limit the differentiation or culture step in claim 39.

Claim 182 is indefinite because it does not further limit claim 161 which already requires the cells are cultured in conditioned medium.

Claim 183 is indefinite because the cells of claims 39 and 160 already have telomeric activity and thus appear to express telomerase.

Claim 184 is indefinite because it is unclear how longer telomeres is an indication of “telomeric activity" and because it is unclear how to compare to any “differentiated cell" as claimed. The stem cells from adipose tissue themselves are “differentiated cells” as claimed because they are not totipotent.

Claim 185 is indefinite because the metes and bounds of what applicants consider "self-renewing" is unclear.

Claim 186 is indefinite because it cannot further limit a method of differentiation to indicate the stem cells can be cultured for at least 15 passages without differentiating. If applicants are attempting to set forth a step, the step should be clearly set forth. If applicants are attempting to set forth a function of the stem cells, it is unclear how the phrase distinguishes the function or structure from stem cells capable of only being cultured for less than 15 passages.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39-42, 44, 45, 47, 57, 160-162, 169-173 and 179-186 are rejected under 35 U.S.C. 102(e) as being anticipated by Gimble (US Patent 6,555,374).

The effective filing date of Gimble is Aug. 19, 1999, the filing date of Provisional Application 60/149,849.

Gimble isolated stem cells from adipose tissue and differentiated them into bone cells (col. 16, Example 5) and skeletal muscle myoblasts (Examples 7 and 8) and smooth muscle cells (Example 9). Gimble used methods that also caused differentiation into adipocytes (col. 13, lines 13-16). The stem cells isolated from adipocytes exposed to 5' azacytidine (Example 7, col. 19, line 4) inherently differentiated into chondrocytes because exposure to 5' azacytidine causes differentiation into chondrocytes (col. 2, lines 12-21).

The "clonally isolated" cells claimed encompass a "heterogeneous population of clonally isolated cells" (claim 179), which are equivalent to the stem cells separated from the adipose tissue described by Gimble. The stem cells of Gimble are also "clonally isolated" as claimed because i) Gimble differentiated clonal stem cells into skeletal muscle myoblasts (col. 19, line 9-10) and ii) Gimble taught the stem cells of the invention included clonally isolated stem cells (col. 1, lines 39-45). It is noted Gimble discussed differentiating clonal mouse embryo stem cell lines (C3H10T1/2 or 3T3) into cells having adipocyte, myocyte, chondrocyte or osteoblast morphology (col. 2, lines 12-25).

The stem cells inherently have “telomeric activity” (claims 39, 160) or “express telomerase" (claim 183) because telomerase is expressed in cells that divide regularly or at low levels in a cycle-dependent manner and because the stem cells were dividing regularly in culture. Claim 184 is included because it is indefinite.

Without evidence to the contrary, the myocytes inherently are “capable of spontaneous contractile activity” as in claim 2 and “capable of aligning with and exhibiting synchronous contractile activity with a plurality of cardiac cells when grafted into a ventricular myocardium” as in claim 48 because they have myocytic potential.

Claims 57, 179, 180 are included because they are indefinite.

The media described by Gimble is “conditioned” as in claim 161 (Table 3, caption “1:25 or 1:125 diluted conditioned medium”).

Claims 169-171 are included because they further limit the muscle cell of claim 39 but do not exclude differentiating the cells into fat and bone cells. Claim 171 is also included because the muscle cells of Gimble inherently express myoD or myosin heavy chain.

Claim 172 is included because Gimble grew the cells in pre-adipocyte medium; “pre-adipocyte” is a “precursor of a fat cell” as claimed.

Claim 173 is included because the media comprised growth factors.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39-42, 44, 45, 47, 57, 160-162, 169-173 and 179-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gimble (US Patent 6,555,374) in view of Halvorson (US Patent 6,153,432), Park (Bone, June 1999, Vol. 24, pg 549-554), Kirkland (Obesity Res., 1993, Vol. 1, No. 2, pg 87-91), Constantinides (Nature, May 1977, Vol. 267, pg 366-368) and Jones (Cell, 1980, Vol. 20, pg 85-93).

This rejection assumes Gimble does not differentiate the "clonally isolated" stem cells described in Example 7 into at least two types of cells selected from the group consisting of fat, bone, chondrocytes and muscle cells.

The effective filing date of Gimble is Aug. 19, 1999, the filing date of Provisional Application 60/149,849.

Gimble isolated stem cells from adipose tissue and differentiated them into bone cells (col. 16, Example 5) and skeletal muscle myoblasts (Examples 7 and 8) and smooth muscle cells (Example 9). Gimble used methods that also caused differentiation into adipocytes (col. 13, lines 13-16). The stem cells isolated from adipocytes exposed to 5' azacytidine (Example 7, col. 19, line 4) inherently differentiated into chondrocytes because exposure to 5' azacytidine causes differentiation into chondrocytes (col. 2, lines 12-21).

The stem cells inherently have "telomeric activity" as claimed because telomerase is expressed in cells that divide regularly or at low levels in a cycle-dependent manner and because the stem cells are dividing regularly in culture.

Without evidence to the contrary, the myocytes inherently are "capable of spontaneous contractile activity" as in claim 2 and "capable of aligning with and exhibiting synchronous contractile activity with a plurality of cardiac cells when grafted into a ventricular myocardium" as in claim 48 because they have myocytic potential.

Claims 57, 179, 180 are included because they are indefinite.

The media described by Gimble is "conditioned" as in claim 161 (Table 3, caption "1:25 or 1:125 diluted conditioned medium").

Claims 169-171 are included because they further limit the muscle cell of claim 39 but do not exclude differentiating the cells into fat and bone cells. Claim 171 is also included because the muscle cells of Gimble inherently express myoD or myosin heavy chain.

Claim 172 is included because Gimble grew the cells in pre-adipocyte medium; "pre-adipocyte" is a "precursor of a fat cell" as claimed.

Claim 173 is included because the media comprised growth factors.

Gimble differentiated clonal stem cells obtained from adipose tissue into skeletal muscle myoblasts (col. 19, line 9-10), but Gimble did not differentiate the clonal stem cells described in Example 7 into cells other than myocytes.

However, Gimble taught the stem cells of the invention included clonally isolated stem cells (col. 1, lines 39-45), and Gimble discussed differentiating a clonal mouse embryo stem cell line (C3H10T1/2 or 3T3) into cells having adipocyte, myocyte, chondrocyte or osteoblast morphology (col. 2, lines 12-25). In addition, Gimble taught the conditions required to differentiate stem cells obtained from adipose tissue into bone cells (col. 16, Example 5; col. 17, lines 1-5), skeletal muscle myoblasts (Examples 7 and 8), smooth muscle cells (Example 9) and adipocytes (col. 13, lines 13-16). Furthermore, the conditions required to differentiate stem cells isolated from adipose tissue into adipocytes were described by Halvorsen (col. 10, line 59), cited by Gimble in col. 13, line 15, and were well known in the art at the time of filing as described by Kirkland (pg 88, col. 2, "differentiation of human preadipocytes").

Thus, it would have been obvious to those of ordinary skill in the at the time of filing to differentiate clonal stem cells obtained from adipose tissue described by Gimble into myocytes as described by Gimble in Example 7 and also differentiate the clonal cells into adipocytes and osteocytes using the adipogenic or osteogenic medium described by Gimble or into adipocytes using adipogenic medium described by Halvorsen and Kirkland. Those of ordinary skill in the art at the time of filing would have been motivated to differentiate the clonally isolated stem cells described by Gimble in Example 7 into adipocytes or osteocytes using adipogenic or osteogenic medium described by Gimble, Halvorsen or Kirkland to obtain adipocytes and osteocytes and to establish a pluripotent clonal stem cell.

Those of ordinary skill in the art at the time of filing would have had a reasonable expectation of success in differentiating clonal stem cells obtained from adipose tissue described by Gimble into at least two cell types selected from the group consisting of adipogenic, osteogenic and myogenic cells because Gimble taught clonal stem cells obtained from adipose tissue differentiated into myocytes and non-clonal stem cells obtained from adipose tissue differentiated into osteogenic and adipogenic cells and because Kirkland taught clonal stem cells obtained from adipose tissue differentiated into adipocytes. Further support is provided by Park who taught cloned adipocyte stem cells obtained from bone marrow differentiate into adipocytes and osteocytes (abstract, “Cloned adipocytes were found to … …differentiate into two morphologically distinct cell types: osteoblasts and adipocytes in appropriate culture systems"). Clonal pluripotent adipocyte stem cells were known to exist in the bone marrow (Park), so those of skill

would have had a reasonable expectation of obtaining a clonal pluripotent adipocyte from adipose tissue. Accordingly, those of ordinary skill in the art at the time of filing would have had a reasonable expectation of isolating a clonal stem cells obtained from adipose tissue that differentiated into myocytes as described by Gimble in Example 7 and adipocytes or osteocytes using the media described by Gimble or Halvorsen. Those of ordinary skill would have simply screened for clones that differentiated into at least two cell types.

If Gimble did not teach cloning stem cells, methods of cloning pluripotent stem cells were well-known in the art at the time of filing as described by Constantinides and Jones who used the mouse embryonic stem cell lines C3H10T1/2 or 3T3. More particularly, cloning stem cells obtained from adipose tissue that differentiated into adipocytes was specifically taught by Kirkland (pg 89, lines 4-7).

Accordingly, it would have been obvious to those of ordinary skill in the at the time of filing to differentiate stem cells obtained from adipose tissue described by Gimble using clonally isolated stem cells. Those of ordinary skill in the art at the time of filing would have been motivated to use clonally isolated stem cells instead of non-clonal stem cells to establish a cell line having uniform characteristics. Those of ordinary skill in the art at the time of filing would have had a reasonable expectation of success in cloning the stem cells described by Gimble because such methods were well known in the art at the time of filing.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The cells of U.S. Patent No. 6,777,231 were found to be patentably distinct from the methods claimed in the restriction requirement sent 11-2-04.

The cells of U.S. Patent No. 7,470,537 were found to be patentably distinct from methods of differentiation as claimed in the restriction requirement sent in application 10/740315 on 11-2-05.

The cells of U.S. Patent Application 10/651564 are similarly patentably distinct from the methods claimed.

The methods of differentiating stem cells obtained from adipose tissue into perivascular tissue in application 11/995408 are patentably distinct from the method claimed.

Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims 45, 52, 85 and 92 of copending Application No. 10/845315. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap significantly. The method claimed in the instant application could have been claimed in '315 and vice versa. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 11/211114. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap significantly. The method claimed in the instant application could have been claimed in '114 and vice versa. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-40 of copending Application No. 12/066348. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap significantly. The method claimed in the instant application could have been claimed in '348 and vice versa. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 39-42, 44, 45, 47, 48, 57, 160-162 and 169-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-54 of copending Application No. 12/315967. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap significantly. The method claimed in the instant application could have been claimed in '967 and vice versa. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Gronthos (J. Cellular Physiology, 2001, Vol. 189, pg 54-63) has been considered under art. Gronthos isolated human adipose tissue-derived stromal cells (ADSC) (pg 59, table 4) and differentiated them under osteogenic and adipogenic conditions to obtain bone and fat cells (pg 56, col. 1). The ADSC are "clonally isolated" as claimed because they have been separated from the adipose tissue and are "stem cells" as claimed because they are pluripotent. The ADSC have "telomeric activity" as claimed because they are normal cells from patients between 23-58 years old. Cells from patients between 23-58 inherently have normal telomerase activity. However, Gronthos is not available as prior art because the effective filing date of the claims is 3-10-00, the

filing date of PCT/US00/06232; the disclosure of the PCT is the same as the instant application.

This action is non-final.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

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